

B1
Cordt
propoxy-5-methane-sulfonylamidophenyl)-1,5-dihydropyrazolo[3,4-*d*]pyrimidin-4-one and
1-cyclopentyl-3-ethyl-6-(3-ethoxy-4pyridyl)-pyrazolo[3,4-*d*]pyrimidin-4-one.

Please add new Claims 30-33 as follows:

- B2
- 30. A method of treating sexual dysfunction which comprises administering by inhalation an effective amount of 5-[2-ethoxy-5-(4-methylpiperazinylsulfonyl)phenyl]-1-methyl-3-*n*-propyl-1,6-dihydro-7*H*-pyrazolo[4,3-*d*]-pyrimidin-7-one in an atomisable composition or a finely divided particulate form to a subject in need of such treatment. --
 - 31. A medicament comprising 5-[2-ethoxy-5-(4-methylpiperazinylsulfonyl)phenyl]-1-methyl-3-*n*-propyl-1,6-dihydro-7*H*-pyrazolo[4,3-*d*]-pyrimidin-7-one in an atomisable composition or a finely divided particulate form. --
 - 32. A medicament according to Claim 31, in which the atomisable composition is an aerosol comprising said inhibitor in solution or dispersion in a propellant or a nebulizable composition comprising a dispersion of said inhibitor in an aqueous or aqueous/organic medium. --
 - 33. A medicament according to Claim 31, in which said inhibitor in finely divided particulate form is inhaled together with a particulate carrier. --

REMARKS

Favorable consideration of this application is respectfully requested in view of the foregoing amendment and the following remarks.

Claims 21-33 are pending in the application. Claims 21-29 have been rejected. Claims 22-24 have been cancelled without prejudice. Claim 21 has been amended. New Claims 30-33 are supported throughout the specification. No new matter has been added.

I. The Rejection of Claims 21-24, 26-27 and 29 Under 35 U.S.C. §103(a), May Properly Be Withdrawn

Claims 21-24, 26-27 and 29 have been rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,077,841 (see Sui et al.). Before addressing the rejection based on this reference, a brief summary of the invention as defined in amended independent Claim 21 is stated below.

Amended independent Claim 21 is directed to a method of treating sexual dysfunction which comprises administering by inhalation an effective amount of an inhibitor in an atomisable composition or a finely divided particulate form. The inhibitors are selected from the group consisting of 5-[2-ethoxy-5-(4-methylpiperazinyl-sulfonyl)phenyl]-1-methyl-3-*n*-propyl-1,6-dihydro-7*H*-pyrazolo[4,3-*d*]-pyrimidin-7-one, 4-phenylmethylamino-6-chloro-2-(1-imidazolyl)quinazoline, 4-phenyl-methylamino-6-chloro-2-(3-pyridyl)-quinazoline, 1,3-dimethyl-6-(2-propoxy-5-methanesulfonylamidophenyl)-1,5-dihydropyrazolo[3,4-*d*]pyrimidin-4-one and 1-cyclopentyl-3-ethyl-6-(3-ethoxy-4pyridyl)-pyrazolo[3,4-*d*]pyrimidin-4-one.

These specific inhibitors are particularly beneficial to the user since they exhibit maximum concentration in plasma in a very short time when they are delivered to the lungs. For example, in Example 93 the concentration of sildenafil was shown to reach a maximum within 5 minutes after intratracheal administration to a rat and in Example 94 sildenafil was shown to reach a maximum concentration in plasma within 2 minutes after intratracheal administration to a rat.

Sui et al. is directed to the use of 5-heterocyclyl pyrazolopyrimidinones and derivatives thereof for the treatment of male erectile dysfunction (ED). In particular, Sui et al. in the background section describe the shortcomings of utilizing the phosphodiesterase V (PDEV) inhibitor, sildenafil and related analogs, as an orally effective medication to treat ED, i.e., that sildenafil and analogs thereof have less efficacy in patients who had undergone a radical prostatectomy and that they possess undesirable side effects including headache, flushing and disrupted color vision (see column 2, lines 3-13). To address these shortcomings, Sui et al. describe an alternative class of PDEV inhibitors, 5-heterocyclyl pyrazolo-pyrimidines (5-HPs) to treat ED. While Sui et al. indicate that 5-HPs can be administered through various routes including inhalation, the reference does not teach or suggest that sildenafil, or its analogs can also be administered in inhalable form, the form such an inhalable product would take and how such form of sildenafil would be prepared. Indeed, Sui et al., in its disclosure of the shortcomings of sildenafil in orally administrable form and its provision of 5-HPs in place of sildenafil or its related analogs, discourage the use of sildenafil and its analogs in its orally administrable form let alone in inhalable form. Additionally, Sui et al. does not teach or suggest any of the other compounds recited in amended Claim 21, that such compounds can also be administered by inhalation, the form that such compounds would take or how they would be prepared.

The Examiner in rejecting these claims has asserted that one of ordinary skill in the art would have been motivated to select a group of compounds and a specific form of administration from the choices taught by Sui et al. to provide more options to health providers and patients and for its marketing purposes. In response, Applicants note that the medication is taken to enable the

user to achieve or maintain an erection for sexual intercourse so one skilled in the art would expect the market instead to demand a more discrete method of administration. To this end, Sui et al. acknowledges (column 1, lines 51-59) that mechanical devices are not favored and tend to be used only as a last resort. Sui et al. also acknowledges (column 1, lines 60 through column 2, lines 16) that sildenafil as an orally administrable medication has been welcomed by patients despite causing side effects as discussed above. In not disclosing the form of the inhalable 5-HP product or its preparation, and by exemplifying oral administration of 5-HP Sui et al. recognizes that the market is demanding oral administration. If the market is demanding an effective orally administrable treatment where is the motivation to develop an inhalable seldafil or other compounds recited in amended Claim 21?

In view of the lack of teaching or suggestion in Sui et al. that sildenafil or the other compounds recited in amended Claim 21 can be effectively administered by inhalation, and the market demand for an orally administrable treatment for ED rather than use of a mechanical device, one skilled in the art would not have been motivated to develop seldanafil and the other compounds of amended Claim 18 in inhalable form to treat ED.

Accordingly, Sui et al. does not make obvious Claims 21-24, 26-27 and 29. In view of the above, withdrawal of the rejection of Claims 21-24, 26-27 and 29 under 35 U.S.C. §103 is respectfully requested.

II. The Rejection of Claims 25 and 28 Under 35 U.S.C. §103(a) May Properly Be Withdrawn

Claims 25 and 28 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Sui et al. in view of U.S. Patent No. 5,225,183 (see Purewal et al.).

With respect to Sui et al., Applicant reiterates the arguments proffered with respect to addressing the rejection of Claims 21-24, 26-27 and 29.

Purewal et al. is directed to an aerosol formulation which utilizes a particular propellant, 1,1,1,2-tetrafluoromethane, as an ozone-friendly alternative to deliver bronchodilator drugs and steroids to the airways of asthmatic patients. While Purewal et al. describe different types of medicaments that can be utilized with this formulation, it does not teach or suggest that any of the specific compounds recited in amended Claim 21 can be utilized in such a formulation to treat ED.

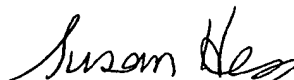
Accordingly, since one skilled in the art reading Sui et al. would not have been motivated to utilize an inhalable form of the specific compounds recited in Claim 21, and Purewal merely teaches the use of an ozone-friendly propellant in an aerosol formulation, the combination of Sui et al. and Purewal does not make obvious Claims 25 and 28.

In view of the above, withdrawal of the rejection of Claims 25 and 28 under 35 U.S.C. §103(a) is respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "APPENDIX. Marked-Up Version of the Changes Made".

A good faith effort has been made to place the present application in condition for allowance. If the Examiner believes that a telephone conference would be of value, he is requested to call the undersigned counsel at the number listed below.

Respectfully submitted,



Susan Hess
Attorney for Applicant
Reg. No. 37,350
(862) 778-7859

Novartis
Patent and Trademark Dept.
One Health Plaza, Bldg. 430
East Hanover, NJ 07936

SH/ld

Attach.: Appendix

Date: December 11, 2002

APPENDIX

Marked-Up Version of the Changes Made

IN THE CLAIMS:

Claims 22-24 have been cancelled without prejudice.

Claim 21 has been amended as follows:

21. (amended) A method of [treatment] treating [of] sexual dysfunction which comprises administering by inhalation an effective amount of an inhibitor of cGMP PDE 5 in an atomisable composition or a finely divided particulate form to a subject in need of such treatment, wherein said inhibitor is selected from the group consisting of 5-[2-ethoxy-5-(4-methylpiperazinyl-sulfonyl)phenyl]-1-methyl-3-*n*-propyl-1,6-dihydro-7*H*-pyrazolo[4,3-*d*]-pyrimidin-7-one, 4-phenylmethylamino-6-chloro-2-(1-imidazolyl)quinazoline, 4-phenyl-methylamino-6-chloro-2-(3-pyridyl)-quinazoline, 1,3-dimethyl-6-(2-propoxy-5-methane-sulfonylamidophenyl)-1,5-dihydropyrazolo[3,4-*d*]pyrimidin-4-one and 1-cyclopentyl-3-ethyl-6-(3-ethoxy-4pyridyl)-pyrazolo[3,4-*d*]pyrimidin-4-one.